Implications of biosafety recommendations on derivation of influenza vaccine reference virus and vaccine manufacture

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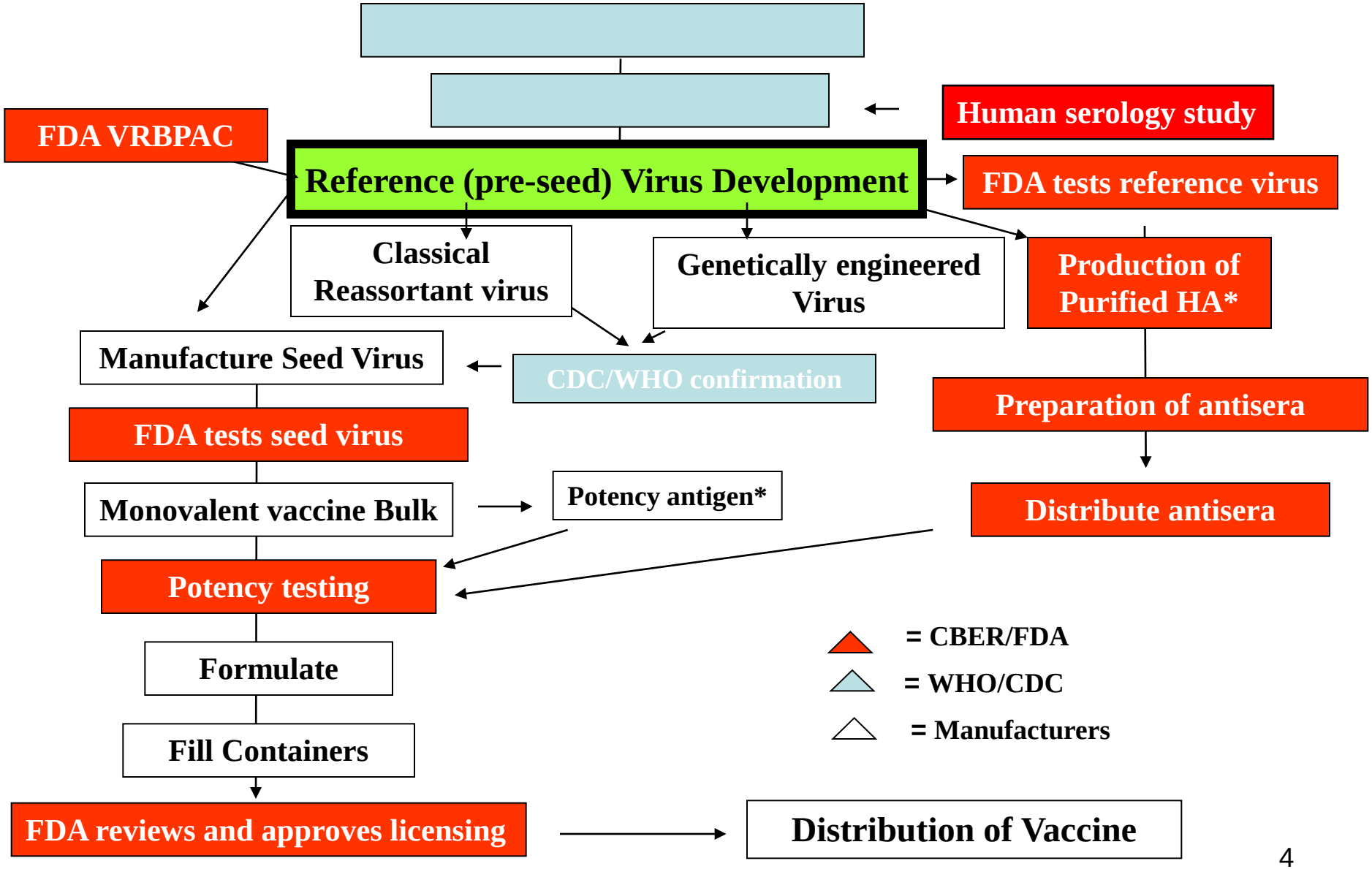
Development of Pandemic Influenza Vaccine Reference Viruses

- Development of representative candidate influenza vaccine reference viruses is coordinated by WHO and is an ***essential component of global pandemic preparedness***
- Newly emerging viruses are compared by antigenicity and genetic relationship to candidate vaccine viruses
- Based on available antigenic, genetic and epidemiologic data, new candidate vaccine viruses are proposed by WHO
- Institutions preparing and distributing candidate vaccine reference viruses:
  - CDC, USA
  - CDC/NIV (National Institute of Virology), USA/India
  - FDA/CBER, USA
  - NIBSC (National Institute for Biological Standards and Control) UK
  - NIID (National Institute of Infectious Diseases) Japan
  - SJCRH (St Jude Children's Research Hospital) USA

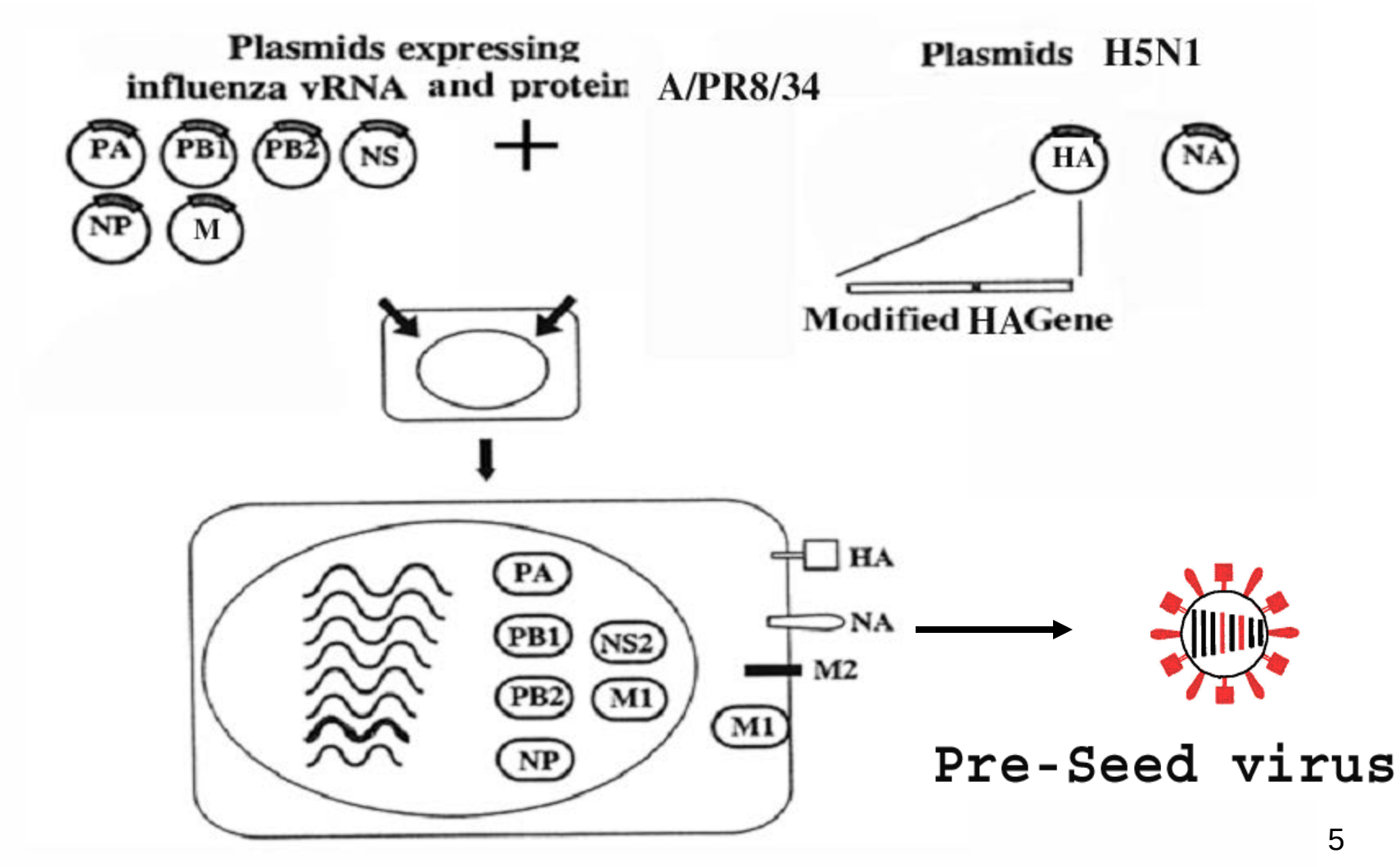
Steps in the Generation of an H5N1 Reference Virus

- Receive highly pathogenic avian influenza (HPAI) virus in WHO Coordinating Center (CC) or Essential Regulatory Laboratory
  - Pre-pandemic viruses may be highly pathogenic but not highly transmissible among humans
  - An emerging pandemic virus will be highly transmissible and probably highly pathogenic
  - WT viruses considered for candidate vaccine development may or may not be resistant to antivirals
- Genetically modify HPAI virus to Low PAI by Reverse Genetic (RG) method under BSL3+ containment
- Conduct safety tests on modified reference virus
- Apply for and receive USDA exclusion from 9 CFR part 121 (Select Agent) to enable distribution to manufactures for vaccine production

CBER/FDA's Roles in Vaccine Preparation and licensing Inactivated Pandemic Vaccine



Rescue of non-pathogenic H5N1 reassortant influenza vaccine strain by Reverse Genetics (RG) method



Safety Tests for Pandemic Vaccine Strains

Inability to plaque in absence of trypsin

Egg embryo survival

Chicken pathogenicity

Ferret pathogenicity - attenuated relative to parental strains

Mice pathogenicity - attenuated relative to parental strains

Available and Proposed Candidate A(H5N1) Vaccine Viruses

Status of influenza A(H5N1) candidate vaccine virus development (September 2012)

Candidate vaccine viruses	Clade	Institution*	Available
A/Viet Nam/1203/2004 (CDC-RG; SJRG-161052)	1	CDC and SJCRH	Yes
A/Viet Nam/1194/2004 (NIBRG-14)	1	NIBSC	Yes
A/Cambodia/R0405050/2007 (NIBRG-88)	1.1	NIBSC	Yes
A/duck/Hunan/795/2002 (SJRG-166614)	2.1	SJCRH	Yes
A/Indonesia/5/2005 (CDC-RG2)	2.1.3.2	CDC	Yes
A/bar-headed goose/Qinghai/1A/2005 (SJRG-163222)	2.2	SJCRH	Yes
A/chicken/India/NIV33487/2006 (IBCDC-RG7)	2.2	CDC/NIV	Yes
A/whooper swan/Mongolia/244/2005 (SJRG-163243)	2.2	SJCRH	Yes
A/Egypt/2321-NAMRU3/2007 (IDCDC-RG11)	2.2.1	CDC	Yes
A/turkey/Turkey/1/2005 (NIBRG-23)	2.2.1	NIBSC	Yes
A/Egypt/N03072/2010 (IDCDC-RG29)	2.2.1	CDC	Yes
A/Egypt/3300-NAMRU3/2008 (IDCDC-RG13)	2.2.1.1	CDC	Yes
A/common magpie/Hong Kong/5052/2007 (SJRG-166615)	2.3.2.1	SJCRH	Yes
A/Hubei/1/2010 (IDCDC-RG30)	2.3.2.1	CDC	Yes
A/barn swallow/Hong Kong/D10-1161/2010 (SJ-003)	2.3.2.1	SJCRH	Yes
A/chicken/Hong Kong/AP156/2008 (SJ-002)	2.3.4	SJCRH	Yes
A/Anhui/1/2005 (IBCDC-RG6)	2.3.4	CDC	Yes
A/duck/Laos/3295/2006 (CBER-RG1)	2.3.4	FDA	Yes
A/Japanese white eye/Hong Kong/1038/2006 (SJRG-164281)	2.3.4	SJCRH	Yes
A/goose/Guiyang/337/2006 (SJRG-165396)	4	SJCRH	Yes
A/chicken/Viet Nam/NCVD-016/2008 (IDCDC-RG12)	7.1	CDC	Yes
A/chicken/Viet Nam/NCDV-03/2008 (IDCDC-RG25A)	7.1	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Institution**	**Availability**
A/chicken/Bangladesh/11RS1984-30/2011-like	2.3.4.2	CDC	Pending
A/Indonesia/NIHRD11771/2011-like	2.1.3.2	NIID	Pending